RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1, 20-22, 27, 31-33, 35, 37-41, 43, 45, 49-52, and 54 were pending. Claim 20 is amended to correct a minor typographic error. No new matter is added. Claims 45 and 49 are canceled without prejudice. Claims 1, 20-22, 27, 31-33, 35, 37-41, 43, 50-52, and 54 are presented herein for reconsideration. Applicants note that the currently pending claims all relate to use of dark lighting conditions in methods of inducing formation of embryogenic cotton callus from non-embryogenic cotton callus.

B. Rejections Under 35 U.S.C. § 103(a)

The Action rejects claim 1 as obvious over Finer (Canadian Patent 1,309,367) in view of Rangan *et al.* (U.S. Patent 5,834,292), and claims 20-22, 27, 31-33, 35, 37-41, 43, 45, 49-52, and 54 as obvious over Finer in view of Rangan, further in view of combinations of Davis (*In Vitro* 9:395-398, 1974), Chi *et al.* (*Pl. Cell Rep.* 9:195-198, 1990), Klimaszewska *et al.* (U.S. Patent 6,200,809), Rangan 1993 (U.S. Patent 5,244,802), and Perlman (U.S. Patent 5,341,557). Applicants respectfully traverse.

(1) Rejection of claim 1 in view of Finer and Rangan (1998)

(a) Neither Finer nor Rangan demonstrate production of embryogenic callus under dark conditions

Applicants respectfully submit that neither Finer nor Rangan (U.S. Patent 5,834,292) show use of dark lighting conditions, for instance as in claim 1, to allow for improved tissue culture efficiency. Importantly, at page 15, bottom, Finer states that the described media, *i.e.* in all of the subsequent examples, is utilized with a 16:8 hour light:dark photoperiod. Thus, not only are all examples in Finer written in the present tense, *i.e.* prospectively, but the examples are also

contemplated as being performed in alternating **light**:dark photoperiods, *i.e.* without dark conditions. Thus, not only does Finer provide **no actual results** that demonstrate obtention of embryogenic callus following growth under dark conditions, or improved efficiency in obtaining embryogenic callus by tissue culture performed under dark conditions as is presently claimed, but the examples cited do not even contemplate actual use of dark conditions. At most, Finer provides only a most general teaching for how culture may be performed, while explicitly stating that light is preferred (*e.g.* Finer, page 8, lines 1-2: "...preferably induced in the light"). In fact, Finer **teaches away** from the claimed invention.

Rangan likewise does not perform callus culture in dark conditions, and only uses dark conditions for seed germination (*e.g.* column 6, line 65, or column 11, line 54). Once explants are prepared, they are grown in callus growth medium in a 16:8 light:dark photoperiod, *i.e.* also without dark conditions (*e.g.* starting at column 7, line 1; also see column 8, line 29, column 10, line 35; and column 11, line 62).

Finer also provides no teachings regarding induction of embryogenesis for non-embryogenic callus in dark conditions (*e.g.* other than 16:8 light:dark photoperiod). Thus, Finer does not teach or suggest that, for instance, dark culture conditions are beneficial during growth on an embryogenesis-inducing medium in order to yield embryogenic callus from non-embryogenic callus. Thus the present results discussed in section (d) below are clearly unexpected in view of the lack of teachings of Finer in this regard.

Simply put, **neither Finer nor Rangan recognize or teach that dark culture conditions are a result-effective variable** for improving embryogenesis, for instance, as to the timing of a dark culture step during one or more of his steps (a)-(c), before or during embryogenesis induction. (M.P.E.P. 2144.05 (II) (B)). Thus, the presently claimed invention is non-obvious. Brief mention is

made of dark conditions at page 8, line 1, for step (a) of the Finer protocol, during initial (non-embryogenic) callus induction, although alternating light:dark is preferred. However, Finer again **prefers lighted conditions** instead of dark conditions during steps (b)- (c), such as during step (b) at page 9, 2nd paragraph, and page 10, 4th paragraph. Thus, in view of Finer, a practitioner would not expect that dark culture is beneficial during induction of embryogenesis since: (1) use of a 16 hour photoperiod is generally preferred (*e.g.* page 9, 1st full paragraph); (2) a 16 hour photoperiod is contemplated in all (prospective) examples (page 15, bottom); (3) Finer's discussion regarding use of dark conditions in steps (a)- (c) does not distinguish between non-embryogenic (*e.g.* initial callus induction) and embryogenic growth; and, as noted above, (4) no actual results regarding use of dark culture are given. If anything, at page 9, 2nd paragraph or page 10, 4th paragraph, Finer is **teaching away** from induction of embryogenesis under dark conditions.

In contrast, the present Specification, for instance at page 6, lines 6-30, notes that transgenic non-embryogenic callus obtained from cotton hypocotyl is to be cultured on an induction medium to promote formation of embryogenic callus **in the dark**. Examples 2 and 9 of the present Specification further **specifically demonstrate enhanced efficiency for use of dark culture during embryogenesis** (*e.g.* Example 2, Table 2 at page 26; and Example 9, *e.g.* 1st section of Table 11 at page 34). Applicants note that "protocol 1" of present Example 9 uses embryo induction with a 16:8 hour light:dark photoperiod, while "protocol 2" of Example 9, which demonstrated enhanced embryogenesis, refers back to Example 2 for induction of embryogenesis (*e.g.* Specification, page 33, line 16), and utilizes dark conditions at that time. In view of the above, withdrawal of the obviousness rejection is respectfully requested.

(b) The Finer reference is apparently understood in a manner which contradicts its own teachings

The Action asserts at page 3, 3rd paragraph, that the explant Finer used "for the induction of cotton callus was hypocotyl (p.4, last par. And p. 5, 2nd par.)." However, Applicants notes that this portion of Finer **does not state that the callus induced from hypocotyl was embryogenic callus**, only referring to it as "callus". Indeed, nowhere in Finer is any embryogenic callus actually shown to be produced from a hypocotyl explant by his methods. The Action at page 3, 2nd to last line, asserts that Finer's callus of Example 2 which proliferated on their medium 2 was then placed in Medium #3. Applicants again respectfully note that **this hypocotyl-derived callus is not described as being embryogenic**. Additionally, Finer's callus tissues of Example 3, which were subsequently placed in Medium #4 in order to form embryos, are **not described as being hypocotyl-derived**, and it is unclear how they were obtained. However, in view of Finer's teaching that hypocotyl-derived callus is unorganized while callus from somatic embryos is organized (page 7, 5th paragraph), Applicants submit that the callus of Example 3, which is placed in Medium #4, is presumably derived from embryos instead of hypocotyls. Otherwise the examples would not be discussing any use of callus derived from somatic embryos, **which is explicitly his most preferred source of obtaining embryogenic callus**, and this would contradict the teachings of Finer at p. 5, 3rd paragraph. That is, the Action's apparent understanding of Finer's Examples 2-4 as showing that only hypocotyl-derived callus was utilized to obtain embryogenic callus contradicts the teaching in Finer, at page 5, 3rd paragraph, that callus from somatic embryos is **most preferred** for obtaining embryogenic callus, and would also ignore Finer's teaching at page 7, 5th paragraph, that callus from hypocotyls was unorganized (*i.e.* non-embryogenic), while callus from somatic embryos is embryogenic. Thus, the Action's assertion, for instance at page 5, 1st full paragraph, that Finer teaches a method "of inducing the formation of regenerable embryogenic cotton callus tissue from hypocotyl under dark lighting conditions" is not supported. In view of this, Applicants respectfully

submit that the Action's apparent understanding of Finer is mistaken. Withdrawal of the rejection is therefore requested.

(c) Use of dark lighting conditions for embryogenesis does not represent routine experimentation

The Action at pages 4-5 also asserts that Rangan teaches culture of cotton explants to initially yield undifferentiated callus, which is then grown further until embryogenic callus is formed. Applicants note that these cited portions of Rangan (*e.g.* column 8, lines 15-67) **explicitly describe this callus culture as taking place in a 16:8 light dark photoperiod** and not under dark conditions. Thus, use of dark conditions for embryogenesis, as presently claimed, is not being taught here. Instead, if anything, Rangan is teaching away from use of dark conditions by specifying that an alternating light:dark photoperiod is to be used. The Action, at page 5, also apparently considers that culturing callus in the dark would be a routine choice of experimental design and would prevent greening of callus tissue.

However, Applicants respectfully submit that such an assertion regarding a choice of light duration during a step of embryogenesis represents **hindsight** reasoning, as it is only one parameter among numerous other tissue culture parameters which might be studied, and a skilled worker would have had no expectation that varying such a particular parameter would lead to enhanced embryogenesis, or that greening of callus tissue affects induction of embryogenesis. "A particular parameter must first be recognized as a result-effective variable, *i.e.*, a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. M.P.E.P. 2144.05 (II) (B). Since the parameter(s) of light duration during embryogenesis were not recognized in either cited reference as being result-effective and amenable to optimization, Applicants respectfully submit that selecting such a parameter would **not** represent routine experimentation.

Although Rangan is asserted at page 4 in the Action in view of its teachings regarding transformation rather than embryogenesis, Applicants note that following the initial germination of cotton seed in the dark (*e.g.* column 6, line 65; or column 8, line 13), **subsequent tissue culture steps in Rangan are stated to be carried out under 16:8 light:dark photoperiods** (*e.g.* Rangan, column 7, line 10; column 8, line 30; column 9, line 47; column 10, line 35; column 11, line 62; column 25, line 67; column 26, line 20). Thus, no use of dark lighting conditions in a method to produce transformed embryogenic cotton callus is taught or suggested by Rangan, and the addition of Rangan to Finer, if anything, also teaches away from use of dark conditions, instead further demonstrating that alternating light:dark photoperiods are to be used. Additionally, the Action asserts that Example 26 of Rangan describes results of transformation of cotton to plants. As discussed in the telephonic interview, Applicants respectfully submit that Rangan's Example 26 (as well as Example 18 to which it refers), does not describe transformed callus as giving rise to transformed plants. Instead, this portion of Rangan only states that callus could be transformed, and that transformed callus could be selected, or that plant segments could be transformed, and transformed callus selected from those explants, without showing that such callus was embryogenic or that embryogenic callus could advantageously be produced via dark culture conditions to ultimately yield transformed plants. Thus, the teachings of Rangan with regard to transformation do not cure this defect in Finer regarding use of dark conditions to obtain embryogenic callus from hypocotyl explants, as presently claimed.

Applicants also respectfully reiterate that it is unclear why Rangan is combined with Finer regarding transformation, yet Rangan's teachings regarding use of a 16 hour photoperiod are being, apparently, arbitrarily disregarded, among the numerous potential experimental conditions, and combinations of experimental conditions, that might be utilized to enhance embryogenesis. For

instance, the efficacy of one or more other parameters relating to tissue source, developmental stage, age, size; and numerous potential media components, among other parameters, might just as well have been studied by a skilled worker interested in enhancing embryogenesis from cotton callus. One could literally envision millions of different combinations of variables to use. Applicants thus respectfully submit that this is a *prima facie* demonstration of **hindsight reasoning** by the Action.

Even if, only *in arguendo*, varying the parameters of light intensity/duration during a step of induction of callus embryogenesis were to be considered "obvious to try," Applicants note that "obvious to try" is **not equivalent** to obvious, and also bring to the Examiner's attention *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988) as summarized in *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009):

> To differentiate between proper and improper applications of 'obvious to try,' this court outlined two classes of situations where '**obvious to try' is erroneously equated with obviousness under § 103**. In the first class of cases,
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> > what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. [*In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988]
>
> *Id.* In such circumstances, where a defendant merely throws **metaphorical darts at a board filled with combinatorial prior art possibilities**, courts should not succumb to hindsight claims of obviousness."

[*In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009, at p. 14; emphasis added] Applicants respectfully submit that the Action's assertions are tainted with just such hindsight reasoning, since neither piece of cited art gives any indication that callus culture under dark conditions can lead to any benefit, particularly for embryogenesis of hypocotyl-derived callus tissue. Further, Applicants respectfully reiterate that 11 years apparently passed between the priority dates of Finer and of the present Application (circa 1988- 1999), and Applicants submit that this likewise demonstrates that use of

dark culture conditions was not an obvious parameter for a skilled artisan to alter in order to improve embryogenesis. In support of this, Applicants note that Rangan with a priority date of 1998 did not alter their lighting parameters to a dark culture regime. Therefore, culture of hypocotyl-derived cotton callus tissue under dark lighting conditions to obtain regenerable embryogenic callus tissue is not obvious in view of the cited references, and withdrawal of the rejection is respectfully requested.

(d) The present application demonstrates unexpected results regarding embryogenesis under dark conditions

In contrast to the shortcomings of the prior art, Applicants have surprisingly and unexpectedly shown that use of dark lighting conditions leads to an enhanced rate of formation of embryogenic hypocotyl-derived cotton callus. For instance, see Specification at Example 2 starting at page 25, including Tables 2-3; and Example 9 including Table 11; as well as the enclosed Inventor's Declaration under 37 C.F.R. §1.132. As discussed in the Declaration, neither Finer, nor Finer in view of Rangan, would lead a skilled worker to use of dark conditions to allow for rapid embryogenesis of hypocotyl-derived callus, especially in view of the numerous potential culture parameters, and combinations of parameters, which might be varied even if such a goal were being pursued with hypocotyl tissues.

The present Application provides ample experimental results demonstrating the effect of dark culture conditions, either alone or in combination with other experimental parameters, in enhancing embryogenesis of hypocotyl-derived callus. For instance, Example 2 starting at page 25, and including Tables 2-3, demonstrates that dark conditions allow for a 2X-5X fold increase in the proportion of explant pieces that develop embryogenic callus, as compared to use of a 16 hour photoperiod. Examples 3-7 and 9 of the present Application further show how dark culture may be utilized in conjunction with other parameters in methods to enhance embryogenesis as well as to

enhance the efficiency of later steps in producing embryos, maturing them, and germinating them to yield plantlets. Likewise, Example 9, beginning at page 33 illustrates the unexpected nature and degree of improvement described in the present Application. As discussed in Example 9, Protocol 1 from Example 1, utilized a 16:8 day:night cycle (*e.g.* Specification, page 25, line 15, and page 34, line 3), while Protocol 2 utilized a period of incubation in the dark as described in Example 2, as well as other modified parameters of Examples 3, 5, 6, and 8. Table 11 demonstrates substantial improvement in frequency of embryogenic calli (*e.g.* increase of from 12% to 45% when comparing protocols 1 and 2). The possibility of such an improvement in embryogenesis rate as well as its rapidity, via use of dark culture conditions is neither taught nor suggested by Finer in view of Rangan. In view of these **unexpected results**, withdrawal of the rejection of claim 1 made in view of these references is respectfully requested.

(e) The Action fails to take into account all claims limitations

At page 10, 2nd paragraph, the Action asserts that certain features of Applicant's invention (*i.e.* that dark conditions are beneficial during induction of embryogenesis) which are being relied upon in Applicant's arguments, are not recited in the rejected claims. Applicants traverse, and respectfully note that present claim 1 explicitly recites a method for inducing formation of embryogenic cotton callus tissue by culturing non-embryogenic callus tissue under dark conditions and obtaining embryogenic callus tissue therefrom. Withdrawal of the rejection is therefore respectfully requested.

(2) Rejections of claims 20-22, 27, 31-33, 35, 37-41, 43, 45, 49-52, and 54

The Action rejects claims 20-22, 27, 31-33, 35, 37-41, 43, 45, 49-52, and 54 over Finer in view of Rangan, further in view of combinations of Davis (*In Vitro* 9:395-398, 1974), Chi *et al.* (*Pl. Cell Rep.* 9:195-198, 1990), Klimaszewska *et al.* (U.S. 6,200,809), Rangan 1993 (U.S. 5,244,802),

and Perlman (U.S. 5,341,557). Applicants respectfully traverse while noting that claims 45 and 49 are canceled, and their rejection in view of Perlman is thus moot. None of the additional references cure the defects in Finer, or in Finer in view of Rangan, as discussed above, in that all of these claims relate to use of dark conditions for culturing non-embryogenic callus, to obtain embryogenic callus therefrom. Additionally, the accompanying Declaration of Inventors under 37 C.F.R. §1.132 demonstrates that the result of use of dark conditions for induction of embryogenesis is surprising and unexpected. Withdrawal of these rejections is therefore respectfully requested.

D. Conclusion

In view of the above, it is submitted that all of the rejections to the claims have been overcome, and the case is in condition for allowance. The Examiner is invited to contact the undersigned at (214) 259-0932 with any questions, comments, or suggestions relating to the referenced patent application.

Respectfully submitted,

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